```
=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:36:14 ON 18 OCT 2002)
L24          45 DUP REM L23 (23 DUPLICATES REMOVED)

=> d que 124
L1            1 SEA FILE=REGISTRY ARGINYLGLUTAMINE/CN
L2       445578 SEA FILE=REGISTRY RQ/SQSP
L3          981 SEA FILE=REGISTRY SQL=2
L4            7 SEA FILE=REGISTRY L2 AND L3
L5            8 SEA L1
L6            7 SEA L4
L7          610 SEA NEU J?/AU
L9         1460 SEA ARGIN?(A) GLUTAMIN?
L11           1 SEA L7 AND DIPEPTID?
L12        1475 SEA L5 OR L6 OR L9
L13         340 SEA L12 AND (NUTRIENT# OR NUTRIT?)
L14          30 SEA L13 AND (MUSCL? OR MUSCU?)
L15         182 SEA L13 AND (IMMUNO? OR IMMUNI? OR IMMUNE?)
L16          16 SEA L15 AND PATHOGEN?
L17          44 SEA L15 AND (BACTERI? OR FUNG? OR YEAST# OR PARASIT?)
L18          90 SEA L15 AND INFECT?
L20           3 SEA L17 AND DIPEPTID?
L21           4 SEA L18 AND DIPEPTID?
L22          53 SEA L14 OR L16 OR L20 OR L21 OR L11
L23          68 SEA L22 OR L5 OR L6
L24          45 DUP REM L23 (23 DUPLICATES REMOVED)


=> d ibib abs 124 1-45

L24  ANSWER 1 OF 45  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:676157  HCAPLUS
DOCUMENT NUMBER:          137:226599
TITLE:                    Small peptides capable of modulating the bioadhesion
                          and signal transduction functions of CD66 (CEACAM)
                          family members
INVENTOR(S):              Skubitz, Keith M.; Skubitz, Amy P. N.
PATENT ASSIGNEE(S):       USA
SOURCE:                   PCT Int. Appl., 96 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2002068601      A2   20020906       WO 2002-US5720    20020227
         W:  JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
PRIORITY APPLN. INFO.:                    US 2001-272113P  P  20010228
AB   The present invention relates to peptides capable of modulating the
     function (e.g., signaling or adhesive activities) of CD66 (CEACAM) family
     members and/or their ligands.  Specifically, a series of peptides derived
     from functional domains of CD66 antigens are used to modulate
     CD66-mediated cell adhesion or signal transduction.
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Search completed by David Schreiber  308-4292

L24 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:155620 HCAPLUS
DOCUMENT NUMBER: 136:166576
TITLE: Physiological action of amino acids. Cystine
AUTHOR(S): Kishi, Kyoichi; Nikawa, Takeshi; Rokutan, Kazuhito
CORPORATE SOURCE: Sch. Med., The Univ. Tokushima, Japan
SOURCE: Rinsho Eiyo (2002), 100(2), 150-154
CODEN: RNEYAW; ISSN: 0485-1412
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on the physiol. functions of amino acids, regulation of gene expression by amino acids, therapeutic use of amino acids ( **arginine**, **glutamine**, branched chain amino acids, etc.), **nutritional** effects of cysteine, physiol. functions of taurine and glutathione, and effects of cystine and cysteine on the **muscle** injury under exercise, **muscle** atrophy, and oxidative stress injury in rats.

L24 ANSWER 3 OF 45 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002055906 MEDLINE
DOCUMENT NUMBER: 21640555 PubMed ID: 11781377
TITLE: **Nutrients** and their role in host resistance to infection.
AUTHOR: Field Catherine J; Johnson Ian R; Schley Patricia D
CORPORATE SOURCE: Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Canada.. Catherine.Field@ualberta.ca
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (2002 Jan) 71 (1) 16-32.
Ref: 224
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020131
Entered Medline: 20020130
AB Almost all **nutrients** in the diet play a crucial role in maintaining an "optimal" **immune** response, such that deficient and excessive intakes can have negative consequences on **immune** status and susceptibility to a variety of **pathogens**. Iron and vitamin A deficiencies and protein-energy malnutrition are highly prevalent worldwide and are important to the public health in terms of **immunocompetence**. There are also **nutrients** (i.e., **glutamine**, **arginine**, fatty acids, vitamin E) that provide additional benefits to **immunocompromised** persons or patients who suffer from various infections. The remarkable advances in **immunology** of recent decades have provided insights into the mechanisms responsible for the effects of various **nutrients** in the diet on specific functions in **immune** cells. In this review, we will present evidence and proposed mechanisms for the importance of a small group of **nutrients** that have been demonstrated to affect host resistance to infection will be presented. An inadequate status of some of these **nutrients** occurs in many populations in the world

(i.e., vitamin A, iron, and zinc) where infectious disease is a major health concern. We will also review **nutrients** that may specifically modulate host defense to infectious **pathogens** (long-chain polyunsaturated n-3 fatty acids, vitamin E, vitamin C, selenium, and nucleotides). A detailed review of the effect of long-chain polyunsaturated n-3 fatty acids on host defense is provided as an example of how the disciplines of **nutrition** and **immunology** have been combined to identify key mechanisms and propose **nutrient** -directed management of **immune**-related syndromes.

L24 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935662 HCAPLUS
DOCUMENT NUMBER: 136:58855
TITLE: Chemically-modified peptides, compositions, and methods of production for antimicrobial use
INVENTOR(S): Kuhner, Carla H.; Romesser, James A.
PATENT ASSIGNEE(S): Hercules Incorporated, USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001098362 | A2 | 20011227 | WO 2001-US19400 | 20010615 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001068512 | A5 | 20020102 | AU 2001-68512 | 20010615 |
| PRIORITY APPLN. INFO.: | | | US 2000-212441P | P 20000616 |
| | | | WO 2001-US19400 | W 20010615 |

OTHER SOURCE(S): MARPAT 136:58855
AB Compns. and methods for inhibiting and controlling the growth of microbes are disclosed. The compn. comprises at least one chem.-modified peptide with antimicrobial activity and at least one carrier. The method comprises administering an amt., effective for the prevention, inhibition and termination of microbial growth for industrial, pharmaceutical, household and personal care use.

L24 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833364 HCAPLUS
DOCUMENT NUMBER: 136:595
TITLE: Antitumor pore-forming procytotoxic peptides
INVENTOR(S): Yu, Xianxhang; Wagner, Thomas E.
PATENT ASSIGNEE(S): Greenville Hospital System, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001085777 | A2 | 20011115 | WO 2001-US40690 | 20010509 |
| WO 2001085777 | A3 | 20020307 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-203063P P 20000509
US 2000-212042P P 20000616

OTHER SOURCE(S): MARPAT 136:595

AB A class of procytotoxic agents is characterized by a capability to kill with target cell-specificity. Such an aspect can be a pore-forming protein which has at least one lysine residue, modified by a peptide linkage to an amino acid residue, via the epsilon amino group. These agents are useful in treating cancer, esp. prostate cancer.

L24 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:464362 HCAPLUS
DOCUMENT NUMBER: 135:71283
TITLE: Peptides and compounds that bind to a thrombopoietin receptor for treating thrombocytopenias
INVENTOR(S): Dower, William J.; Barrett, Ronald W.; Cwirla, Steven E.; Gates, Christian M.; Schatz, Peter J.; Balasubramanian, Palaniappan; Wagstrom, Christopher R.; Hendren, Richard Wayne; Deprince, Randolph B.; Podduturi, Surekha; Yin, Qun
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: U.S., 128 pp., Cont.-in-part of U.S. Ser. No. 699,027, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6251864 | B1 | 20010626 | US 2000-516704 | 20000301 |
| WO 9640750 | A1 | 19961219 | WO 1996-US9623 | 19960607 |

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM

PRIORITY APPLN. INFO.: US 1995-478128 B2 19950607
US 1995-485301 B2 19950607
WO 1996-US9623 A2 19960607
US 1996-699027 B2 19960815

AB Described are peptides and peptide mimetics that bind to and activate the thrombopoietin receptor. Such peptides and peptide mimetics are useful in methods for treating hematol. disorders and particularly, thrombocytopenia resulting from chemotherapy, radiation therapy, or bone marrow

transfusions as well as in diagnostic methods employing labeled peptides and peptide mimetics.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:446516 HCAPLUS
DOCUMENT NUMBER: 135:120323
TITLE: Multiple organ failure
AUTHOR(S): Ono, Satoshi; Mochizuki, Hidetaka
CORPORATE SOURCE: 1st Dep. Surg., Natl. Def. Med. Coll., Japan
SOURCE: Rinsho Eiyo (2001), 98(7, Rinjizokan), 924-930
CODEN: RNEYAW; ISSN: 0485-1412
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 12 refs. on **pathogenesis** of multiple organ failure (MOF) or multiple organ dysfunction syndrome (MODS) and management of **nutrition** of MODS patients for supplementation of energy and maintenance of **immune** system. Administration of **glutamine**, **arginine**, .omega.-3 highly unsatd. fatty acids, and growth hormone, and effects of the **nutrients** to the patients are discussed in detail.

L24 ANSWER 8 OF 45 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002245961 MEDLINE
DOCUMENT NUMBER: 21982263 PubMed ID: 11986003
TITLE: Ileal absorptive adaptation to jejunal resection and extrinsic denervation: implications for living-related small bowel transplantation.
AUTHOR: Tsiotos G G; Kendrick M L; Libsch K; Bierens K; Lankisch P; Duenes J A; Sarr M G
CORPORATE SOURCE: Gastroenterology Research Unit and Department of Surgery, Mayo Clinic and Mayo Foundation, 200 First Street SW, Rochester, MN 55905, U.S.A.
CONTRACT NUMBER: R01 39337
SOURCE: JOURNAL OF GASTROINTESTINAL SURGERY, (2001 Sep-Oct) 5 (5) 517-24.
Journal code: 9706084. ISSN: 1091-255X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020503
Last Updated on STN: 20020620
Entered Medline: 20020619
AB Net absorption of water, electrolytes, and simple **nutrients** decreases early after jejunoileal autotransplantation (extrinsic denervation) in a canine model but recovers toward normal by 8 weeks. However, the ability of the extrinsically denervated ileum to adapt after total jejunectomy, which would be relevant as a model of segmental small bowel transplantation, remains unknown. Two groups of five dogs each were studied before and 2 weeks and 12 weeks after 50% proximal enterectomy. A control group remained neurally intact, whereas the other group underwent extrinsic denervation (Ext Den) of the remaining ileum. Using a perfusion technique, net absorption of water, electrolytes, and five simple **nutrients** (glucose, **arginine**, **glutamine**, and oleic and taurocholic acids) was measured at the three time points. Ileal

morphometry was also evaluated. All dogs developed diarrhea, which resolved by 12 weeks in all but two of the Ext Den dogs. Weight in both groups was decreased at 2 weeks ($P < 0.05$), returned to normal at 12 weeks in control dogs, but remained low in Ext Den dogs ($P < 0.05$). Maximal weight loss was greater in the Ext Den group ($P < 0.05$). No consistent or important differences in net absorptive fluxes of water, electrolytes, or simple **nutrients** were noted either within or between groups at any time point. Villous height, crypt depth, and longitudinal **muscle** width increased significantly at 12 weeks after jejunectomy in the Ext Den dogs, but not in the control dogs ($P < 0.05$). Extrinsic denervation of the ileum results in persistent weight loss after proximal 50% enterectomy. Despite diarrhea, only minor changes in electrolyte absorption occur, and ileal net absorption of simple **nutrients** remains unaffected. The ileum of extrinsically denervated dogs undergoes a more prominent morphometric adaptation after jejunectomy. Extrinsic denervation necessitated by small bowel transplantation, independent of immune effects, does not appear to suppress the ileal adaptive response to maintain net absorption of water, electrolytes, and simple **nutrients**.

L24 ANSWER 9 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:296975 BIOSIS
DOCUMENT NUMBER: PREV200100296975
TITLE: Acute reduction in dexamethasone-induced weight loss with alanyl-glutamine **dipeptide** supplementation in artificially reared rat pups.
AUTHOR(S): DeMarco, Vincent G. (1); Tremper, Kate (1); Singleton, Kristen (1); **Neu, Josef (1)**
CORPORATE SOURCE: (1) Pediatrics, University of Florida, Gainesville, FL USA
SOURCE: Pediatric Research, (April, 2001) Vol. 49, No. 4 Part 2, pp. 298A. print.
Meeting Info.: Annual Meeting of the Pediatric Academic Societies Baltimore, Maryland, USA April 28-May 01, 2001
ISSN: 0031-3998.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L24 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2002:99828 HCAPLUS
DOCUMENT NUMBER: 136:294009
TITLE: **Nutrition** and **immune** function
AUTHOR(S): Calder, Philip C.
CORPORATE SOURCE: Institute of Human Nutrition, School of Medicine, University of Southampton, Southampton, S016 7PX, UK
SOURCE: Nutrition Clinique et Metabolisme (2001), 15(4), 286-297
CODEN: NCMEEV; ISSN: 0985-0562
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review. A major deficiency of dietary energy or of one or more essential **nutrients**, including vitamins A, B6, B12, C, and E, folic acid, zinc, iron, copper, selenium, essential amino acids, and essential fatty acids, can impair **immune** functions and increase host susceptibility to infectious **pathogens**. This is most likely because these **nutrients** are involved in the mol. and cellular responses to challenges of the **immune** system. Providing these **nutrients** to deficient individuals can restore

**immune** functions and improve resistance to infection. Thus, appropriate **nutrition** is required for the host to maintain adequate **immune** defenses towards bacteria, viruses, fungi, parasites, and tumor cells. Although the intakes of several **nutrients** which result in greatest enhancements of **immune** functions appear to be greater than the recommended intakes, excess intakes of certain **nutrients** can also impairs **immune** responses. Some **nutrients** (**glutamine**, **arginine**) may become limiting in crit. illness and their provision may aid in patient recovery.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 4

ACCESSION NUMBER: 2001:761033 HCAPLUS
DOCUMENT NUMBER: 136:261971
TITLE: Nitrogen nutraceuticals: from test tube to clinical practice
AUTHOR(S): Cynober, L.
CORPORATE SOURCE: Laboratoire de Biochimie A et INSERM U431, Hotel-Dieu, Paris et Laboratoire de Biologie de la Nutrition. EA 2498. Faculte de Pharmacie Paris V, F75181, Fr.
SOURCE: Cahiers de Nutrition et de Dietetique (2001), 36(4), 273-284
CODEN: CNDQA8; ISSN: 0007-9960
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review. The so-called **immunopharmaconutrients** are amino acids which display regulatory metabolic properties independent of the nitrogen they contain. Typically, **glutamine**, **arginine**, and their common precursor ornithine .alpha.-ketoglutarate enter this category. These amino acids modulate protein turnover and contribute to gut trophicity and **immune** cell functionality. Besides a huge no. of exptl. and bioclin. studies, recent trials indicate that glutamine (in a free form or as **dipeptides**) given by the parenteral route, and enterally administered arginine, decrease the frequency of **infection** and the stay at the hospital in intensive care unit patients. Ornithine .alpha.-ketoglutarate exhibits a marked action on wound healing in burn patients and post-operative patients (head and neck cancer). The underlying mechanisms of action remain unclear. However, it is likely that the actions of these amino acids are mediated in part through their metab. (into nitric oxide, glutathione, polyamines) through increased hormone secretions (Insulin, growth hormone) and through cell swelling. This issue is complexed by the fact that **glutamine**, **arginine** and ornithine .alpha.-ketoglutarate are metabolically linked. The large splanchnic metab. of glutamine explains the low efficacy of this amino acid when given enterally and also when used in elderly patients. At the turn of the millennium, it is clear that providing a **glutamine**-, **arginine**-, or ornithine .alpha.-ketoglutarate-enriched diet is indicated in subgroups of catabolic patients. However, there are few data allowing to choose one of these mols. rather than the others. Pharmacol. speaking, avoiding any mixt. of these mols. at random, every new product must be carefully validated comparing its efficacy to the appropriate isonitrogenous control.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER: 2001:517976 HCAPLUS
DOCUMENT NUMBER: 135:303158
TITLE: Nitrogen pharmaconutrients: from the test tube to clinical practice
AUTHOR(S): Cynober, Luc
CORPORATE SOURCE: Laboratoire de Biochimie A, Hotel Dieu, Paris, 75181, Fr.
SOURCE: Nutrition Clinique et Metabolisme (2001), 15(2), 131-143
CODEN: NCMEEV; ISSN: 0985-0562
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review with 142 refs. **Immunopharmaconutrients** are amino acids with regulatory metabolic properties independent of the nitrogen they are bringing to the body. **Glutamine, arginine,** and their common precursor ornithine .alpha.-ketoglutarate (Cetornan, Ornicetil) are typically put into this category. These amino acids modulate protein turnover and are contributive to the gut trophicity and **immune** cell functionality. Recent trials indicate that parenterally given glutamine (free or in **dipeptides**) and enterally given arginine decrease the incidence of **infections** and the length of hospital stay in intensive care unit patients. Ornithine .alpha.-ketoglutarate is effective in wound healing in burn patients and post-operative patients (head and neck cancer). The underlying mechanisms of action remain unclear. The actions of these amino acids may be mediated partly through their metab. (into nitric oxide, glutathione, polyamines), through increased secretion of hormones (insulin, growth hormone), and through cell swelling. This issue is complex due to the fact that **glutamine, arginine,** and ornithine .alpha.-ketoglutarate are metabolically linked. The extensive splanchnic metab. of glutamine explains the low efficacy of this amino acid when given enterally and perhaps when used in elderly patients. Providing diets enriched with **glutamine, arginine,** or ornithine .alpha.-ketoglutarate may be indicated in catabolic patients. There are few data allowing the choice of one of these compds. over the others, thus any random mixt. of these mols. should be avoided. Every new product from this category must be carefully validated and compared for its efficacy with appropriate isonitrogenous controls.

REFERENCE COUNT: 142 THERE ARE 142 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:388523 HCAPLUS
DOCUMENT NUMBER: 133:54545
TITLE: Sequences of retinoblastoma(Rb) and E2F fusion proteins and the therapeutic uses thereof for hyperproliferative disorders
INVENTOR(S): Antelman, Douglas; Gregory, Richard J.; Wills, Kenneth N.
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: U.S., 87 pp., Cont.-in-part of U.S. Ser. No. 751,517, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6074850 | A | 20000613 | US 1997-801092 | 19970214 |
| WO 9821228 | A1 | 19980522 | WO 1997-US21821 | 19971113 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9855899 | A1 | 19980603 | AU 1998-55899 | 19971113 |
| AU 723660 | B2 | 20000831 | | |
| EP 948520 | A1 | 19991013 | EP 1997-952238 | 19971113 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO | | | | |
| BR 9712767 | A | 19991026 | BR 1997-12767 | 19971113 |
| CN 1244870 | A | 20000216 | CN 1997-181317 | 19971113 |
| JP 2001503638 | T2 | 20010321 | JP 1998-522958 | 19971113 |
| KR 2000053323 | A | 20000825 | KR 1999-704327 | 19990515 |
| US 6379927 | B1 | 20020430 | US 1999-315113 | 19990519 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1996-751517 | B2 | 19961115 |
| | US 1997-801092 | A | 19970214 |
| | WO 1997-US21821 | W | 19971113 |

AB The present invention relates to the construction of a chimeric gene encoding an E2F fragment contg. DNA binding domain and nonfunctional cyclin A binding domain, and a Rb fragment including a functional growth suppression domain, wherein expression of the chimeric gene results in repressing transcription of E2F promoter, and causes cell cycle arrest in a variety of cell types. The invention also relates to operatively linking the fusion protein encoding DNA with a tissue-specific promoter such as a smooth muscle alpha actin promoter, to direct the tissue-specific cell growth inhibition. The invention further relates to the therapeutic uses of the fusion protein for the treatment of hyperproliferative disorders including cancer and restenosis.

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 45 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:454814 SCISEARCH
THE GENUINE ARTICLE: 323WU
TITLE: Involvement of **glutamine**, **arginine**, and polyamines in the action of ornithine alpha-ketoglutarate on macrophage functions in stressed rats
AUTHOR: Moinard C (Reprint); Caldefie F; Walrand S; Felgines C; Vasson M P; Cynober L
CORPORATE SOURCE: FAC PHARM, LAB BIOL NUTR, 4 AV OBSERV, F-75006 PARIS, FRANCE (Reprint); CTR RECH NUTR HUMAINE, FAC PHARM, LAB BIOCHIM BIOL MOL & NUTR, CLERMONT FERRA, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (JUN 2000) Vol. 67, No. 6, pp. 834-840.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0741-5400.
DOCUMENT TYPE: Article; Journal

Search completed by David Schreiber 308-4292

FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The ability of ornithine alpha-ketoglutarate (OKG) to enhance macrophage cytotoxicity in stress situations has been described, but the mechanisms involved remain unclear. It is known that OKG administration generates glutamine (GLN), arginine (ARG), and polyamines. This study will (1) evaluate the effect of OKG on tumor necrosis factor alpha (TNF-alpha) secretion and nitric oxide (NO.) production in macrophages from glucocorticoid (DEX)-treated rats, and determine whether these effects can be reproduced by GLN or ARG supplementations, and (2) use in vivo metabolic inhibitors methionine sulfoximine (inhibitor of GLN synthetase), S-methylthiourea (inhibitor of inducible nitric oxide synthase), and difluoromethylornithine (inhibitor of ornithine decarboxylase) to assess the roles of GLN, ARG, and polyamines in OKG action. Controls received a mixture of nonessential amino acids (NEAA). GLN, ARG, and OKG all restored TNF-alpha secretion by Macrophages of glucocorticoid-treated rats. The same results were obtained with GLN and ARG supplementation However, the use of inhibitors clearly showed that OKG does not modulate TNF-alpha secretion by GLN, ARG, or polyamine pathways. We also observed that OKG enhanced NO. release by stimulated macrophages (DEX-OKG, 1.77 +/- 0.64 vs. DEX-NEAA, 0.29 +/- 0.29 nmol/10(6) cells, $P < 0.05$). Using inhibitors, it appears that this action of OKG is probably mediated via polyamine synthesis and GLN. However, an oral administration of an equimolar amount of GLN failed to reproduce the OKG-mediated effect, possibly because OKG generates more GLN in the systemic circulation than GLN itself when these substances are given orally. Our results underline the complexity of the mechanism of action of OKG, which can differ according to the functions of even a single cell type.

L24 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:821911 HCAPLUS
DOCUMENT NUMBER: 134:130814
TITLE: Neither glutamine nor arginine supplementation of diets increase glutamine body stores in healthy growing rats
AUTHOR(S): Boza, J. J.; Moennoz, D.; Jarret, A. R.; Vuichoud, J.; Garcia-Rodenas, C.; Finot, P. A.; Ballevre, O.
CORPORATE SOURCE: Nestle Research Center, Nestec Ltd., Lausanne, Switz.
SOURCE: Clinical Nutrition (2000), 19(5), 319-325
CODEN: CLNUDP; ISSN: 0261-5614
PUBLISHER: Harcourt Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the work was to resolve whether glutamine and arginine supplemented diets affect plasma and tissue (**muscle**, liver and intestinal mucosa) glutamine concns., as well as glutaminase and glutamine synthetase specific activities. The trial was performed in growing rats fed 10% protein diets for 3 wk. Protein sources were: whey proteins (W); whey proteins + free glutamine (WG); whey proteins + arginine (WA); and casein + wheat protein hydrolyzate + acid whey (39:39:22), as source contg. protein-bound glutamine (CGW). Rats fed the control diet (6.4% glutamine) (W) showed comparable glutamine body stores to those of rats fed the WG diet. In fact, glutamine supplementation down-regulated the hepatic glutamine synthetic capacity of growing rats (W/WG: 6.8 .+-. 0.3 vs 6.0 .+-. 0.2 nmol/min/mg protein). Arginine supplementation of the diet (up to 9% of the protein content) resulted in a decrease in plasma and tissue glutamine concns. (W/WA: plasma, 1218 .+-. 51 vs 1031 .+-. 48

.mu.mol/L; liver 7.5 .+-. 0.4 vs 6.5 .+-. 0.2 .mu.mol/g; **muscle**: 5.7 .+-. 0.2 vs 4.0 .+-. 0.2 .mu.mol/g). These data suggest that glutamine supplementation of the diet does not increase plasma and tissue glutamine concns. in healthy growing rats, while the addn. of arginine to the diet decreases glutamine body stores.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
ACCESSION NUMBER: 2000:450428 BIOSIS
DOCUMENT NUMBER: PREV200000450428
TITLE: Modulation of **immune** response and barrier function in the piglet gut by dietary means.
AUTHOR(S): Bosi, P. (1)
CORPORATE SOURCE: (1) DIPROVAL-Degree of Animal Production Science and Technology, University of Bologna, 42100, Reggio Emilia Italy
SOURCE: Asian-Australasian Journal of Animal Sciences, (July, 2000) Vol. 13, No. Special Issue, pp. 278-293. print. ISSN: 1011-2367.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The knowledge about dietary tools to modulate the **immune** response and barrier function in the piglet gut is still poor. Any method that can lead to an improved feed intake in the first days after weaning, could reduce inflammatory symptoms, improve intestinal morphology and resistance against **pathogens**. After this, a proper choice of raw materials and a correct supply of **nutrients** (**glutamine** , **arginine**, polyamines) can help. Some raw materials (spray-dried whey and spray-dried animal plasma) and additives (bromelain) can have a protective effect against adhesive enterobacteria. Candidate probiotics can be identified by assessing the ability to compete with specific **pathogens** (exclusion of the **pathogen** adhesion to the enterocytes, secretion of bacteriocines, other peptides, acids, strengthening of local **immune** defense), in addition to their ability to develop in the gut. The gut **immune** system is compartmentalized in pig in: a) a diffuse system, intraepithelial (IEL) and in the lamina propria, and in b) organized compartments: Peyer's patches in jejunum and ileum and mesenteric lymph nodes. The contact with microorganisms is an energetic cost, but essential for the maturation of the **immune** system in the gut. The developing knowledge on control mechanism of this system will help to lead to a correct use of probiotics. The effect on the local **immune** system could be: adjuvant effect for a specific antigen administered along with probiotic, lymphocyte proliferation (B and T cells), enhanced cell-mediated **immunity**, enhancement of the innate **immune** system (macrophage phagocytosis), enhanced epithelial cell defense, with induced cell expression of several cell-surface markers of inflammation. The knowledge on modulating molecules of practical use to obtain the same goals is not yet sufficient.

L24 ANSWER 17 OF 45 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:682220 SCISEARCH
THE GENUINE ARTICLE: 350EU
TITLE: Influence of enteral diets supplemented with key **nutrients** on lymphocyte subpopulations in Peyer's patches of endotoxin-boostered mice

Search completed by David Schreiber 308-4292

AUTHOR: Manhart N (Reprint); Vierlinger K; Akomeah R; Bergmeister H; Spittler A; Roth E
CORPORATE SOURCE: UNIV VIENNA, KLIN CHIRURG AKH, CHIRURG FORSCHUNGSLAB, WAHRINGER GURTEL 18-20, A-1090 VIENNA, AUSTRIA (Reprint); UNIV VIENNA, DEPT SURG RES, A-1010 VIENNA, AUSTRIA
COUNTRY OF AUTHOR: AUSTRIA
SOURCE: CLINICAL NUTRITION, (AUG 2000) Vol. 19, No. 4, pp. 265-269

Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 0261-5614.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 27

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background and aims: This study was undertaken to compare the effect of different key **nutrients** on lymphocyte subsets of Peyer's patches (PP) and spleen in endotoxemic mice.

Methods: Female Balb/c mice were fed over a period of 10 days either with an isocaloric and isonitrogenous control diet (Control), a glutamine enriched diet (Diet I) or a diet containing **glutamine**, **arginine**, glycine, and n-3 fatty acids (Diet II). On day 7 the mice were challenged intraperitoneally with 25 mu g LPS. The lymphocyte subpopulations (B cells, T cells, CD4+ and CD8+) of PP and spleen were analysed by flow cytometry. Glutathione content of small intestinal mucosa and spleen was determined by HPLC and luminal small intestinal IgA by ELISA.

Results: Both experimental diets increased the number of B and T cells in the PP and that of T cells in the spleen ($P < 0.01$). Glutathione content in PP and spleen was higher under administration of key **nutrients** ($P < 0.05$). Diet II reduced luminal small intestinal IgA content in comparison to the two other groups.

Conclusion: The addition of arginine, glycine and n-3 fatty acids to a glutamine supplemented diet does not enhance lymphocyte numbers in PP and spleen, but reduces intestinal IgA content. (C) 2000 Harcourt Publishers Ltd.

L24 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:595545 HCAPLUS
DOCUMENT NUMBER: 134:70794
TITLE: **Nutritional** treatment for acquired immunodeficiency virus-associated wasting using .beta.-hydroxy .beta.-methylbutyrate, glutamine, and arginine: a randomized, double-blind, placebo-controlled study
AUTHOR(S): Clark, Robert H.; Feleke, Getachew; Din, Mehraj; Yasmin, Tabassum; Singh, Gurpreet; Khan, Faroque A.; Rathmacher, John A.
CORPORATE SOURCE: Nassau County Medical Center, East Meadow, NY, USA
SOURCE: JPEN, Journal of Parenteral and Enteral Nutrition (2000), 24(3), 133-139
CODEN: JPENDU; ISSN: 0148-6071
PUBLISHER: American Society for Parenteral and EnteralNutrition
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The current study was designed to examine whether a combination of three **nutrients**, consisting of .beta.-hydroxy-.beta.-methylbutyrate

(HMB), a metabolite of leucine, L-glutamine (Gln) and L-arginine (Arg), each of which has been previously shown to slow **muscle** proteolysis, could synergistically alter the course of **muscle** wasting in patients with established acquired immunodeficiency syndrome (AIDS). Sixty-eight human immunodeficiency virus (HIV)-infected patients with a documented wt. loss of at least 5% in the previous 3 mo were recruited from the HIV clinic at Nassau County Medical Center. The subjects were randomly assigned in a double-blind fashion to receive either placebo contg. maltodextrin or the **nutrient** mixt. (HMB/Arg/Gln) contg. 3 g HMB, 14 g L-glutamine, and 14 g L-arginine given in two divided doses daily for 8 wk. Body wts. (BW) were recorded weekly and lean body mass (LBM) and fat mass (FM) were measured by air displacement plethysmog. and by a single computerized tomog. (CT) slice through the thigh at 0, 4, and 8 wk. Forty-three subjects completed the 8-wk protocol, (placebo, n = 21; HMB/Arg/Gln, n = 22). At 8 wk, the subjects consuming the HMB/Arg/Gln mixt. gained 3.0 .+-. 0.5 kg of BW while those supplemented with the placebo gained 0.37 .+-. 0.84 kg (p = .009). The BW gain in the HMB/Arg/Gln-treated subjects was predominantly LBM (2.55 .+-. 0.75 kg) compared with the placebo-supplemented subjects who lost lean mass (-0.70 .+-. 0.69 kg, p = .003). No significant change in FM gain was obsd. (0.43 .+-. 0.83 kg for the group receiving HMB/Arg/Gln and 1.07 .+-. 0.64 kg for the group receiving the placebo, p > .20). Similar percentage changes in **muscle** mass and fat mass were obsd. with CT scans. Immune status was also improved as evident by an increase in CD3 and CD8 cells and a decrease in the HIV viral load with HMB/Arg/Gln supplementation. The data indicate that the HMB/Arg/Gln mixt. can markedly alter the course of lean tissue loss in patients with AIDS-assocd. wasting.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
ACCESSION NUMBER: 2000155594 EMBASE
TITLE: [Importance of supplements following surgical procedures]. BEDEUTUNG VON SUPPLEMENTEN NACH OPERATIONEN.
AUTHOR: Thul P.
CORPORATE SOURCE: Dr. P. Thul, Klin. fur Allgemein-/Thoraxchirurgie, Universitatsklinikum Charite, Campus Mitre, Schumannstrasse 20/21, D-10117 Berlin, Germany. Paul.Thul@Charite
SOURCE: Chirurgische Gastroenterologie mit Interdisziplinaren Gesprachen, (2000) 16/SUPPL. 1 (48-52).
Refs: 33
ISSN: 0177-9990 CODEN: CHGAF6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB A number of supplements were included in the **nutritional** regimen to improve the postoperative outcome after extended abdominal surgical procedures. In the enteral **nutrition glutamine, arginine,** nucleotides and omega-3 fatty acids achieved a more important role. Stable **dipeptides** that are metabolisable to glutamine are available for parenteral **nutrition.** Many clinical studies have shown better nitrogen balances, lower **bacterial** colonisation of the bowel, improved **nutrient** uptake and shorter hospital stay. The **immunological** system is positively influenced

by application of omega-3 fatty acids. In critically ill patients, low levels of antioxidants like vitamins E, C and beta-carotene are detectable. These substances are gaining increasing importance as supplements.

L24 ANSWER 20 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000096759 EMBASE
TITLE: [**Nutrition** in inflammatory bowel disease (Crohn's disease ulcerative colitis) in the chronic stage]. ERNAHRUNG BEI ENTZUNDLICHEN DARMERKRANKUNGEN (MORBUS CROHN, COLITIS ULCEROSA) IM CHRONISCHEN STADIUM.
AUTHOR: Bischoff S.C.; Gastell S.; Martin H.; Ockenga J.; Manns M.P.
CORPORATE SOURCE: Dr. S.C. Bischoff, Med. Hochschule Hannover, Zentrum Innere Medizin/Dermatologie, Abt. Gastroenterologie/Hepatologie, 30623 Hannover, Germany. bischoff.stephan@mh-hannover.de
SOURCE: Viszeralchirurgie, (2000) 35/1 (48-61).
Refs: 121
ISSN: 1435-3067 CODEN: VISZFH
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 048 Gastroenterology
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Malnutrition is frequently observed in patients with inflammatory bowel disease: about 2/3 of all patients with Crohn's disease and 1/3 of those with ulcerative colitis show typical signs of malnutrition. This leads to decrease in weight and specific deficiencies such as anemia, disturbed **immune** functions and osteopenia. In children it can come to less stature, which is untreatedly often irreversible. Therefore, **nutrition**-medical measures should represent a part of the therapy concept with inflammatory bowel disease. Additionally, there are notes for the fact that **nutritional** measures, in particular the artificial **nutrition**, apart from which balance of deficiencies could have also primary-therapeutic meaning, whereby the underlying mechanisms are to large extent unclear. Finally it is assumed that **nutrition** habits and individual food may have etiologic or **pathogenic** meaning for the emergence of inflammatory bowel disease with particular subgroups. While it is unquestionable that **nutrition**-medical measures are of importance in the management of patients with inflammatory bowel disease, there is some disagreement about which strategies are to be preferred. In the acute phase of disease an artificial **nutrition** is recommended, the accurate indication and the type (parenteral or enteral **nutrition**, polymeric or elemental diet etc.) are not defined however. In the remission phase oral **nutrition** forms are the rule. Exceptions can be patients with short bowel syndrome or with fistulae. In recent time new approaches have been suggested and checked such as food formulas containing **immune**-modulating substances (e.g. fish oil, **glutamine**, **arginine**, etc.). Hopeful results have been presented in the meantime for omega-3-fatty acids which cause obviously an extension of the remission phase. While the possible **nutrition** strategies in the acute phase of inflammatory bowel disease have been presented in many works comparatively few outlines are available for **nutrition** in the chronic stage. Therefore the emphasis of the present outline should be the **nutrition** in the chronic stage of inflammatory bowel disease.

L24 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:104502 HCAPLUS

Search completed by David Schreiber 308-4292

DOCUMENT NUMBER: 130:177530
TITLE: Peptides and compounds that bind to a receptor
INVENTOR(S): Dower, William J.; Barrett, Ronald W.; Cwirla, Steven E.; Gates, Christian M.; Schatz, Peter J.; Balasubramanian, Palaniappan; Wagstrom, Christopher R.; Hendren, Richard Wayne; DePrince, Randoph B.; Podduturi, Surekha; Yin, Qun
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: U.S., 126 pp., Cont.-in-part of U.S. Ser. No. 699,027, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5869451 | A | 19990209 | US 1996-764640 | 19961211 |
| WO 9825965 | A2 | 19980618 | WO 1997-EP6850 | 19971209 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9858547 | A1 | 19980703 | AU 1998-58547 | 19971209 |
| AU 725731 | B2 | 20001019 | | |
| ZA 9711045 | A | 19990609 | ZA 1997-11045 | 19971209 |
| EP 948539 | A2 | 19991013 | EP 1997-954363 | 19971209 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CN 1245504 | A | 20000223 | CN 1997-181651 | 19971209 |
| BR 9713914 | A | 20000229 | BR 1997-13914 | 19971209 |
| JP 2001505898 | T2 | 20010508 | JP 1998-526197 | 19971209 |
| US 6121238 | A | 20000919 | US 1999-244298 | 19990203 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1995-478128 | B2 | 19950607 |
| US 1995-485301 | B2 | 19950607 |
| US 1996-699027 | B2 | 19960815 |
| WO 1996-US9623 | A2 | 19960607 |
| US 1996-764640 | A | 19961211 |
| WO 1997-EP6850 | W | 19971209 |

AB Peptides and peptide mimetics are disclosed that bind to and activate the thrombopoietin receptor. The peptides and peptide mimetics are useful in methods for treating hematol. disorders and particularly, thrombocytopenia resulting from chemotherapy, radiation therapy, or bone marrow transfusions, as well as in diagnostic methods employing labeled peptides and peptide mimetics.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:608174 HCAPLUS
DOCUMENT NUMBER: 132:151026
TITLE: Modulation of immune response with ornithine A-ketoglutarate in burn injury: an arginine or glutamine dependency?

Search completed by David Schreiber 308-4292

AUTHOR(S): Le Boucher, J.; Farges, M.-C.; Minet, R.; Vasson, M.-P.; Cynober, L.
CORPORATE SOURCE: INSERM U 402, CHU Saint-Antoine, Paris, Fr.
SOURCE: Nutrition (New York) (1999), 15(10), 773-777
CODEN: NUTRER; ISSN: 0899-9007
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enterally administered ornithine .alpha.-ketoglutarate (OKG) is an efficient complement of **nutritional** support in trauma situations, esp. after burn injury. A typical feature obsd. in this intense catabolic state is insufficient prodn. of glutamine (Gln) and arginine (Arg), two amino acids (AAs) involved in the immune response. As OKG in vivo metab. generates these two AAs, we investigated, in burned rats, the action of OKG with regard to modulation of immunity. Male Wistar rats were randomly allocated to four groups. On day 0, 12 rats were burned with boiling water (20% body surface area). After a 24-h fast, they were enterally refed for 48 h using Osmolite, as a low-calorie low-nitrogen regimen, supplemented with either 5 g OKG/kg/d (n = 6) or an equiv. amt. of nitrogen in the form of glycine (n = 6). Non-burned pair-fed controls treated with glycine (n = 6) and healthy rats fed ad libitum (n = 6) were also studied. Nitrogen balance was assessed from daily measurement of total nitrogen excretion. On day 3, thymus, anterior tibialis **muscle** and proximal jejunum wts. were recorded. **Muscle** and intestinal AA concns. were also quantified. OKG counteracted ($P < 0.01$) the thymic involution that occurs with burn injury, and increased the concns. of Gln and Arg in both the **muscle** ($P < 0.01$ and $P < 0.05$, resp.) and the jejunum ($P < 0.01$ for Gln). When all groups were taken together, a pos. correlation was found between thymus wt. and Gln and Arg **muscle** concns. ($r = 0.71$, $P < 0.001$ and $r = 0.58$, $P < 0.01$, resp.). Furthermore, as expected, OKG improved nitrogen balance. As it is known that total no. of thymocytes parallels thymic wt., and as Gln and Arg are essential **nutrients** for activated immune cells, our results suggest that Gln and Arg derived from OKG are responsible for the immunomodulating properties of this mol. in burn injury.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 2000:39674 HCAPLUS
DOCUMENT NUMBER: 133:30111
TITLE: Amino acid **nutrition** and immune function in tumour-bearing rats: a comparison of **glutamine** -, **arginine**- and ornithine 2-oxoglutarate-supplemented diets
AUTHOR(S): Robinson, Lindsay E.; Bussiere, Francoise I.; Le Boucher, Jacques; Farges, Marie-Chantal; Cynober, Luc A.; Field, Catherine J.; Baracos, Vickie E.
CORPORATE SOURCE: Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, AB, T6G 2P5, Can.
SOURCE: Clinical Science (1999), 97(6), 657-669
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dietary supplementation with glutamine (Gln), arginine (Arg), or ornithine 2-oxoglutarate (ornithine .alpha.-ketoglutarate, OKG) may improve the

anticancer immunity. Female Buffalo rats were fed complete semipurified diets supplemented with Gln, Arg, or OKG for 14 days after implantation of the Morris hepatoma 7777 cells. The control diet was made isonitrogenous and isoenergetic by the addn. of a mixt. of nonessential amino acids. After 14 days, peritoneal macrophages and splenocytes were isolated to det. cell phenotypes, macrophage cytostatic activity, and natural killer (NK) cell cytotoxicity and nitric oxide (NO) and cytokine prodn. The diet had no effect on tumor wt. (1.6.+-.0.2 g). Rats fed OKG had increased macrophage cytostatic activity and NK cell cytotoxicity. Although the enhanced NK cell killing ability was assocd. with higher splenocyte NO prodn., the increased cytotoxicity was not inhibited by the specific inhibitors of inducible NO synthase NG-nitro-L-arginine Me ester (L-NAME) and S-methylisothiourea. The proportion of interleukin-2 receptor-pos. T cells after stimulation increased in rats fed OKG, but cytokine prodn. was not affected by the diet. OKG, Gln, nor Arg altered the tumor growth compared with the control mixt. of nonessential amino acids. The results suggest no net advantage of OKG, Gln, or Arg for anticancer immunity, but do not preclude benefits in immune responses to disease recurrence, metastasis, therapy, or secondary infection.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 9

ACCESSION NUMBER: 1999:518082 HCAPLUS
DOCUMENT NUMBER: 132:35133
TITLE: Phagocyte functions in stressed rats: comparison of modulation by **glutamine**, **arginine** and ornithine 2-oxoglutarate
AUTHOR(S): Moinard, Christophe; Chauveau, Beatrice; Walrand, Stephane; Felgines, Catherine; Chassagne, Jacques; Caldefie, Florence; Cynober, Luc A.; Vasson, Marie-Paule
CORPORATE SOURCE: Laboratoire de Biochimie, Biologie Moleculaire et Nutrition EA 2416 and Centre de Recherche en Nutrition Humaine, Faculte de Pharmacie, Clermont-Ferrand, 63001, Fr.
SOURCE: Clinical Science (1999), 97(1), 59-65
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of diets supplemented with 6.8 mmol/day/kg feed of **glutamine**, **arginine**, or ornithine 2-oxoglutarate [ornithine .alpha.-ketoglutarate (OKG), precursor of both glutamine and arginine] on phagocyte functions measured as H2O2 prodn. by leukocytes and tumor necrosis factor .alpha. (TNF.alpha.) secretion by stimulated macrophages were studied in stressed rats. The relationships between the immunol. effects of these amino acids and their blood plasma and **muscle** and intestine tissue concns. were also explored. The catabolic model used consisted of i.p. injections of dexamethasone (DEX; 1.5 mg/day/kg) for 5 days. DEX suppressed the TNF.alpha. secretion in stimulated macrophages. Addn. of arginine or OKG, but not glutamine, counteracted the DEX effect on TNF.alpha. secretion. **Glutamine**, **arginine**, and OKG increased the H2O2 prodn. by monocytes and polymorphonuclear neutrophils from DEX-treated rats. All DEX-treated rats showed blood plasma and **muscle** glutamine depletion and decreased concns. of arginine in the gastrocnemius **muscle**. **Glutamine**, **arginine**, nor OKG counteracted these depletions. Thus, **glutamine**, **arginine**, and OKG

improve the phagocyte responses during stress. Glutamine depletion is not necessarily assocd. with dysimmunity, since no correlation between glutamine tissue pools and the immune state was obsd.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 25 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999273903 EMBASE
TITLE: [What is the significance of the gut for the etiology of multiorgan failure?].
WELCHE BEDEUTUNG BESITZT DER DARM IN DER ATIOLOGIE DES MULTIORGANVERSAGENS?.
AUTHOR: Weimann A.; Bastian L.; Grotz M.; Heine J.; Schlitt H.J.
CORPORATE SOURCE: Dr. A. Weimann, Klin. Abdominal- Transplant.-chir., Medizinische Hochschule Hannover, Carl-Neuberg-Str. 1, 30625 Hannover, Germany
SOURCE: Aktuelle Ernahrungsmedizin, (1999) 24/1 (20-24).
Refs: 50
ISSN: 0341-0501 CODEN: AEKPDQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
026 Immunology, Serology and Transplantation
048 Gastroenterology
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB At present, the etiology of multiorgan failure is explained by a 'two-hit'-hypothesis considering the gut as a 'motor'. 'Gut injury' with subsequent increase in permeability of the bowel for bacteria and toxins leads to 'priming' of neutrophile granulocytes in the gut. A second injury may produce organ damage by bursting of activated and migrated granulocytes. All these hypotheses are based on animal studies, because in critical illness the bowel eludes appropriate assessment of cellular functions. In patients after abdominal surgery an association was clinically shown between bacterial translocation and an increase in the rate of septic complications. The role of the gut T-lymphocytes system for barrier integrity and function is largely unknown. Experimental results suggest that an activation of intraepithelial lymphocytes might also increase mucosa barrier damage. From the **nutritional** point of view and with regard to the prevention of septic complications and multiorgan failure, the assumed trophic and **immunomodulating** mechanisms in the gut of the new substrates **glutamine**, **arginine**, omega-3-fatty acids and glycine will have to be investigated in greater detail.

L24 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:405986 HCAPLUS
DOCUMENT NUMBER: 129:95717
TITLE: Peptides and compounds that bind to a receptor
INVENTOR(S): Dower, William J.; Barrett, Ronald W.; Cwirla, Steven E.; Gates, Christian M.; Schatz, Peter J.; Balasubramanian, Palaniappan; Wagstrom, Christopher R.; Hendren, Richard Wayne; Deprince, Randolph B.; Podduturi, Surekha; Yin, Qun
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Search completed by David Schreiber 308-4292

FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9825965 | A2 | 19980618 | WO 1997-EP6850 | 19971209 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5869451 | A | 19990209 | US 1996-764640 | 19961211 |
| AU 9858547 | A1 | 19980703 | AU 1998-58547 | 19971209 |
| AU 725731 | B2 | 20001019 | | |
| EP 948539 | A2 | 19991013 | EP 1997-954363 | 19971209 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9713914 | A | 20000229 | BR 1997-13914 | 19971209 |
| JP 2001505898 | T2 | 20010508 | JP 1998-526197 | 19971209 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1996-764640 | A | 19961211 |
| US 1995-478128 | B2 | 19950607 |
| US 1995-485301 | B2 | 19950607 |
| US 1996-699027 | B2 | 19960815 |
| WO 1997-EP6850 | W | 19971209 |

OTHER SOURCE(S): MARPAT 129:95717

AB Peptides (X1IEX2PTLX3X4X5LX6X7X8X9X10)K(X10'X9'X8X7X6LX5X4X3LTPX2EIX1)NH2 [X1 = H, acyl; X2 = G or sarcosine (Sar); X3 = R, A, norleucine, or N-acetyllysine; X4 = Q or E; X5 = W, L-1-naphthylalanine, or F; X6 = A, 5-aminopentanoic acid, or 2-aminobutyric acid; X7 = A, diphenylalanine or is absent; X8 = R, p-aminophenylalanine, N-acetyllysine, or is absent; X9 and X9' are A, .beta.A, N-methylalanine, Sar, or are absent; X10 and X10' are .beta.A or are absent] were prepd. for binding the thrombopoietin receptor (TPO-R). Thus, Fmoc-IE(tBu)GPT(tBu)LR(Pbf)Q(trt)(1-Nal)LAAR(Pbf)(Sar)-OH (Pbf = 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl, trt = trityl, 1-Nal = 1-naphthylalanyl) was prepd. and coupled with lysinamide dihydrochloride (using 2.4 and 1 equiv. of the resp. reactants) to afford H-IEGPTLRQ(1-Nal)LAAR(Sar)-K[(Sar)RAAL(1-Nal)QRLTPGEI]NH2 (AF15705). Peptide AF15705 showed EC50 .ltoreq. 500 nm in TPO-R binding affinity studies.

L24 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:175943 HCAPLUS
DOCUMENT NUMBER: 128:226237
TITLE: Anti-inflammatory peptides and therapeutic uses thereof
INVENTOR(S): Eisenbach-Schwartz, Michal; Beserman, Pierre; Hirschberg, David L.
PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel; Eisenbach-Schwartz, Michal; Beserman, Pierre; Hirschberg, David L.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9809985 | A2 | 19980312 | WO 1997-IL295 | 19970903 |
| WO 9809985 | A3 | 19980507 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6126939 | A | 20001003 | US 1997-864301 | 19970528 |
| AU 9740301 | A1 | 19980326 | AU 1997-40301 | 19970903 |
| EP 927191 | A2 | 19990707 | EP 1997-937794 | 19970903 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001500492 | T2 | 20010116 | JP 1998-512435 | 19970903 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1996-25376P | P | 19960903 |
| US 1996-753141 | A | 19961120 |
| US 1997-864301 | A | 19970528 |
| US 1996-31191P | P | 19961120 |
| WO 1997-IL295 | W | 19970903 |

OTHER SOURCE(S): MARPAT 128:226237

AB The invention is directed to peptides of the formulas (i) Xaa-Yaa-Arg (either Xaa is any amino acid residue and Yaa is Glu or Xaa is absent and Yaa is any amino acid residue with the exception of Pro), (ii) Arg-Yaa-Xaa (either Xaa is any amino acid residue and Yaa is Glu or Xaa is absent and Yaa is any amino acid residue with the exception of Asn), (iii) Xaa-Arg-Yaa (Xaa is any amino acid residue and Yaa is Glu), and (i.v.) Yaa-Arg-Xaa (Xaa is any amino acid residue and Yaa is Glu), and to derivs. thereof, which exert an inhibitory effect on macrophage migration and/or macrophage phagocytic activity. In addn., the peptides and derivs. thereof exert an inhibitory effect on the ability of macrophages and T cells to adhere to extracellular matrix and/or fibronectin. The peptides and derivs. thereof exert an inhibitory effect on a humoral and/or cellular immune response. The invention is also directed to methods for use of the peptides and derivs. thereof and compns. contg. them for the inhibition of inflammation, including but not limited to, inflammation at a joint, in the central nervous system generally, at specific lesions in the central nervous system, and other immune privileged sites. Immune privilege factor was purified from brain conditioned medium and shown to have a similar migration pattern to Glu-Arg.

L24 ANSWER 28 OF 45 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 1999041587 MEDLINE

DOCUMENT NUMBER: 99041587 PubMed ID: 9826214

TITLE: Enteral ornithine alpha-ketoglutarate enhances intestinal adaptation to massive resection in rats.

AUTHOR: Dumas F; De Bandt J P; Colomb V; Le Boucher J; Coudray-Lucas C; Lavie S; Brousse N; Ricour C; Cynober L; Goulet O

CORPORATE SOURCE: Laboratoire de Biochimie A, Hopital Necker AP-HP, Paris, France.

SOURCE: METABOLISM: CLINICAL AND EXPERIMENTAL, (1998 Nov) 47 (11) 1366-71.
Journal code: 0375267. ISSN: 0026-0495.

PUB. COUNTRY: United States

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981202

AB Ornithine alpha-ketoglutarate (OKG) has been advocated in the treatment of critically ill patients for its anabolic effect on protein metabolism. Since OKG is a precursor of **glutamine**, **arginine**, and polyamines, key substrates of intestinal metabolism and function, we investigated the influence of OKG on intestinal adaptation and trophicity and on glutamine status after small bowel resection. After massive (80%) small bowel resection, rats were enterally fed for 7 days with a standard diet supplemented with either OKG (2 g/kg/d) or an isonitrogenous amount of glycine. OKG induced an adaptative hyperplasia of the villi, demonstrated in the jejunum by an increase in the villus height to crypt depth ratio (OKG v control, 4.3+/-0.4 v 3.3+/-0.5, $P < .01$) along with an increase ($P < .05$) in ornithine decarboxylase (ODC) activity (+80%) and ornithine content (+102%). Plasma glutamine (+25%) and **muscle** glutamine (anterior tibialis [AT], +43%; extensor digitorum longus [EDL], +54%) and protein (AT, +32%) were significantly higher ($P < .05$) after OKG administration, supporting its role in the restoration of glutamine pools. In summary, enterally administered OKG, which enhances intestinal adaptation after massive resection and improves **muscle** glutamine and protein content, could contribute significantly to **nutritional** management after small bowel resection.

L24 ANSWER 29 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 11
ACCESSION NUMBER: 1998164903 EMBASE
TITLE: Pharmacological **nutrition** after burn injury.
AUTHOR: De-Souza D.A.; Greene L.J.
CORPORATE SOURCE: D.A. De-Souza, Centro de Quimica de Proteinas, Faculdade de Med. de Ribeirao Preto, Universidade de Sao Paulo, Ribeirao Preto 14049-900, S.P., Brazil
SOURCE: Journal of Nutrition, (1998) 128/5 (797-803).
Refs: 109
ISSN: 0022-3166 CODEN: JONUAI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Burn patients develop pathophysiological alterations, which include extensive nitrogen loss, malnutrition, markedly increased metabolic rate and immunologic deficiency. This predisposes burn patients to frequent infections, poor wound healing, increased length of hospitalization and increased mortality. The **nutritional** support requires high protein and high energy diets preferably administered enterally soon after injury. The effects of increased dietary components such as **glutamine**, **arginine** and (n-3) fatty acids and related compounds have been evaluated in burn victims. These components, when supplied in quantities two to seven times of those in normal diets of healthy persons, appear to have beneficial pharmacological effects on the pathophysiological alterations associated with burns. However, the efficacy of immune-enhancing diets remains to be convincingly shown.

L24 ANSWER 30 OF 45 MEDLINE DUPLICATE 12

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 1998348894 MEDLINE
DOCUMENT NUMBER: 98348894 PubMed ID: 9684269
TITLE: **Immunonutrition**: the pediatric experience.
AUTHOR: Levy J
CORPORATE SOURCE: Children's Digestive Health Center, Columbia University College of Physicians and Surgeons, New York, New York 10032-3784, USA.
SOURCE: NUTRITION, (1998 Jul-Aug) 14 (7-8) 641-7. Ref: 102
Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 19981021
Entered Medline: 19981015

AB The health benefits of specific **nutrients** in the diet are reviewed as they pertain to the pediatric population and its unique needs. Secretory **immunoglobulins**, lysozyme, interferon, and growth factors, among others, are known to confer **immunological** advantages to breast milk. Inhibition of bacterial **pathogens**, as well as permissive growth of a protective colonic ecoflora occur as a result of various cellular and biochemical mechanisms at play. The **immunomodulatory** properties of minerals such as iron, zinc, and selenium, are presented and the newly recognized protective role of vitamin A and its importance in developing countries and in conditions of compromised **nutrition** are discussed. The review also covers the role of **arginine**, **glutamine**, and nucleotides in adaptive responses of the developing gut and in pathologic states such as necrotizing enterocolitis, short bowel syndrome, and inflammatory bowel disease. Probiotics (specific microbial feeds with potential benefits to the host), and prebiotics (dietary components such as complex carbohydrates able to change the colonic microenvironment fostering colonization with non-enteropathogens) are areas of current interest because they offer alternatives for the management of the growing problem of multiple antibiotic resistance and overwhelming infections in the hospitalized patient.

L24 ANSWER 31 OF 45 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:696883 SCISEARCH
THE GENUINE ARTICLE: 117KX
TITLE: Anticatabolic and anabolic strategies in critical illness: A review of current treatment modalities
AUTHOR: Chang D W; DeSanti L; Demling R H (Reprint)
CORPORATE SOURCE: BRIGHAM & WOMENS HOSP, TRAUMA & BURN CTR, 75 FRANCIS ST, BOSTON, MA 02115 (Reprint); BRIGHAM & WOMENS HOSP, TRAUMA & BURN CTR, BOSTON, MA 02115
COUNTRY OF AUTHOR: USA
SOURCE: SHOCK, (SEP 1998) Vol. 10, No. 3, pp. 155-160.
Publisher: BIOMEDICAL PRESS, 1021 15TH ST, BIOTECH PARK STE 9, AUGUSTA, GA 30901.
ISSN: 1073-2322.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 77

Search completed by David Schreiber 308-4292

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Critically ill patients characteristically exhibit a pronounced catabolism in addition to a down-regulation of normal anabolic activity, leading to major complications from loss of body protein stores. The marked decrease in lean body mass and protein stores leads to the loss of essential structural and functional proteins required for restoring and maintaining homeostasis. The standard management of the catabolic response to injury and illness has centered on optimizing **nutrient** intake that modulates but does not reverse the process. Complications of ongoing catabolism therefore remain a major cause of morbidity. Addition of anticatabolic and anabolic agents that may counteract ''the stress response to injury or illness'' may be of significant clinical benefit. Agents currently available for clinical use, which will be described, can be divided into two groups. The first group are **nutrients** and **nutrient** metabolites, namely protein and the specific amino acids, **glutamine**, **arginine**, and branched chain amino acids, especially leucine, The second group are anabolic hormones, namely growth hormone, testosterone, and the testosterone analog oxandrolone. The pros and cons of these agents, as to their anabolic and anticatabolic value, are described.

L24 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:504550 HCAPLUS
DOCUMENT NUMBER: 127:205848
TITLE: Pegylated peptides. V. Carboxy-terminal PEGylated analogs of growth hormone-releasing factor (GRF) display enhanced duration of biological activity in vivo
AUTHOR(S): Campbell, R. M.; Heimer, E. P.; Ahmad, M.; Eisenbeis, H. G.; Lambros, T. J.; Lee, Y.; Miller, R. W.; Stricker, P. R.; Felix, A. M.
CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, USA
SOURCE: Journal of Peptide Research (1997), 49(6), 527-537
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, human growth hormone-releasing factor (hGRF) and analogs were successfully pegylated at the carboxy-terminus using a novel solid- and soln.-phase strategy. Following synthesis, these pegylated hGRF analogs were evaluated for in vitro and in vivo biol. activity. Specifically, hGRF(1-29)-NH2, [Ala15]-hGRF(1-29)-NH2, [des-NH2-Tyr1,D-Ala2,Ala15]-hGRF(1-29)-NH2 and [His1,Val2,Gln8,Ala15,Leu27]-hGRF(1-32)-OH were each C-terminally extended using a Gly-Gly-Cys-NH2 spacer (previously demonstrated not to alter intrinsic biol. activity), and then monopegylated via coupling to an activated dithiopyridyl-PEG reagent. PEG moieties of 750, 2000, 5000 or 10,000 mol. wt. (MW) were examd. to det. the effect of polymer wt. on activity. Initial biol. evaluations in vitro revealed that all C-terminally pegylated hGRF analogs retained high growth hormone (GH)-releasing potencies, regardless of the MW of PEG polymer employed. Two of these pegylated hGRF analogs, [des-NH2-Tyr1,D-Ala2,Ala15]-hGRF(1-29)-Gly-Gly-Cys(NH2)-S-Nle-PEG5000 and [His1,Val2,Gln8,Ala15,Leu27]-hGRF(1-32)-Gly-Cys(NH2)-S-Nle-PEG5000, were subsequently evaluated in both pig and mouse models and found to be highly potent (in vivo potency range = 12-55-fold that of native hGRF). Relative to their non-pegylated counterparts, these two pegylated hGRF analogs exhibited enhanced duration of activity.

L24 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:255323 HCAPLUS
DOCUMENT NUMBER: 126:315676
TITLE: Glutamine and arginine metabolism in tumor-bearing rats receiving total parenteral **nutrition**
AUTHOR(S): Yoshida, Shogo; Ishibashi, Nobuya; Noake, Toshihiro; Shirouzu, Yuichirou; Oka, Toshinori; Shirouzu, Kazuo
CORPORATE SOURCE: First Department of Surgery, School of Medicine, Kurume University, Fukuoka, 830, Japan
SOURCE: Metabolism, Clinical and Experimental (1997), 46(4), 370-373
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Arginine supplementation increases glutamine levels in **muscle** and plasma. Since glutamine prodn. is increased in catabolic states, these observations prompted the authors to investigate whether the flux of arginine to glutamine was increased in tumor-bearing (TB) rats, and the authors measured the synthesis rate of glutamine from arginine in control vs. TB rats receiving std. total parenteral **nutrition** (TPN) soln. Male Donryu rats (N = 36; body wt., 200 to 225 g) were divided into two groups, control and TB rats. Yoshida sarcoma cells (1 .times. 106) were inoculated into the back of the rats s.c. on day 0. The rats were given free access to water and rat chow. On day 5, all animals, including non-TB rats, were catheterized at the jugular vein and TPN was begun. On day 10, TPN soln. contg. either U-14C-glutamine (2.0 .mu.Ci/h) or U-14C-arginine (2.0 .mu.Ci/h) was infused as a 6-h const. infusion. At the end of the isotope infusion, plasma was collected to det. the glutamine prodn. rate in rats receiving U-14C-glutamine, and the ratio of specific activity of glutamine to specific activity of arginine was measured in rats receiving U-14C-arginine. Only 2 g tumor caused a decrease in glutamine levels and an increase in glutamine and arginine prodn. The low flux rate of arginine to glutamine was obsd. in control rats (Arg to Gln, 41.0 .mu.mol/kg/h). TB caused a significant increase in Arg to Gln compared with the control (213.3 .mu.mol/kg/h, v control). An increase in the flux rate of Arg to Gln was assocd. with an enhancement in the ratio of specific activity of ornithine to specific activity of arginine in TB rats (control 51.5% vs. 77.4%). The authors conclude that (1) glutamine and arginine metab. is altered with very small tumors, (2) although the flux of Arg to Gln was increased in TB and rats, the small increase in Arg to Gln cannot explain the obsd. large increase in Gln prodn.

L24 ANSWER 34 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
ACCESSION NUMBER: 1996:417155 BIOSIS
DOCUMENT NUMBER: PREV199699139511
TITLE: Low plasma glutamine in combination with high glutamate levels risk for loss of body cell mass in healthy individuals: The effect of N-acetyl-cysteine.
AUTHOR(S): Kinscherf, R.; Hack, V.; Fischbach, T.; Friedmann, B.; Weiss, C.; Edler, L.; Baertsch, P.; Droege, W. (1)
CORPORATE SOURCE: (1) Div. Immunochem., Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120 Heidelberg Germany
SOURCE: Journal of Molecular Medicine (Berlin), (1996) Vol. 74, No. 7, pp. 393-400.
ISSN: 0946-2716.
DOCUMENT TYPE: Article

LANGUAGE: English

AB Skeletal **muscle** catabolism, low plasma glutamine, and high venous glutamate levels are common among patients with cancer or human immunodeficiency virus infection. In addition, a high glycolytic activity is commonly found in **muscle** tissue of cachectic cancer patients, suggesting insufficient mitochondrial energy metabolism. We therefore investigated (a) whether an "anaerobic physical exercise" program causes similar changes in plasma amino acid levels, and (b) whether low plasma glutamine or high glutamate levels are risk factors for loss of body cell mass (BCM) in healthy human subjects, i.e., in the absence of a tumor or virus infection. Longitudinal measurements from healthy subjects over longer periods suggest that the age-related loss of BCM occur mainly during episodes with high venous glutamate levels, indicative of decreased **muscular** transport activity for glutamate. A significant increase in venous glutamate levels from 25 to about 40 mu-M was seen after a program of "anaerobic physical exercise." This was associated with changes in T lymphocyte numbers. Under these conditions persons with low baseline levels of plasma **glutamine**, **arginine**, and cystine levels also showed a loss of BCM. This loss of BCM was correlated not only with the amino acid levels at baseline examination, but also with an increase in plasma **glutamine**, **arginine**, and cystine levels during the observation period, suggesting that a loss of BCM in healthy individuals terminates itself by adjusting these amino acids to higher levels that stabilize BCM. To test a possible regulatory role of cysteine in this context we determined the effect of N-acetyl-cysteine on BCM in a group of subjects with relatively low glutamine levels. The placebo group of this study showed a loss of BCM and an increase in body fat, suggesting that body protein had been converted into other forms of chemical energy. The decrease in mean BCM/body fat ratios was prevented by N-acetyl-cysteine, indicating that cysteine indeed plays a regulatory role in the physiological control of BCM.

L24 ANSWER 35 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95071930 EMBASE
DOCUMENT NUMBER: 1995071930
TITLE: Recent advances: Parenteral **nutrition** support.
AUTHOR: Mattox T.W.; Bertch K.E.; Mirtallo J.M.; Strausberg K.M.; Cuddy P.G.
CORPORATE SOURCE: Department of Pharmacy, Ohio State University Medical Center, 410 W. 10th Ave.,Columbus, OH 43210, United States
SOURCE: Annals of Pharmacotherapy, (1995) 29/2 (174-180).
ISSN: 1060-0280 CODEN: APHRER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Even though there is an abundance of research related to the clinical and physiologic effects of parenteral **nutrition** and specific **nutritional** substrates, few new products have been released for clinical use. This review illustrates some of the directions being taken in the future development of parenteral **nutrition** products and some new perspectives related to the current effects (or lack of effects) of TPN. When considering the individual effects of specific **nutrient** substrates (**arginine**, **glutamine**, LCTs, MCTs, SCFAs) as reviewed here, it becomes apparent that the infusion

of parenteral **nutrition** has the potential to produce a variety of metabolic responses that could be both beneficial and harmful. These effects depend on the type and quantity of substance infused as well as the disease and clinical condition of the patient. This also is true for those substances (GH, IGF-1) being evaluated to direct the effects of TPN infusions in a manner that improves protein accretion and supports the immunologic response of the body. At best, these investigations are producing a great amount of new and more specific information about the metabolic response to illness and the effects of TPN and individual substrate on that response.

L24 ANSWER 36 OF 45 SCISEARCH COPYRIGHT 2002 ISI (R) DUPLICATE 14
ACCESSION NUMBER: 96:166691 SCISEARCH
THE GENUINE ARTICLE: TW629
TITLE: **NUTRITION** IN PERITONITIS
AUTHOR: ZAZZO J F (Reprint)
CORPORATE SOURCE: HOP ANTOINE BECLERE, SERV ANESTHESIE REANIMAT, 157 RUE PORTE TRIVAUX, F-92141 CLAMART, FRANCE (Reprint)
COUNTRY OF AUTHOR: FRANCE
SOURCE: MEDECINE ET MALADIES INFECTIEUSES, (DEC 1995) Vol. 25, Sp. iss. 1, pp. 86-99.
ISSN: 0399-077X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: French
REFERENCE COUNT: 90

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Peritonitis-induced stress triggers a very sophisticated humoral and metabolic reaction. Inflammatory, immunological and vasoactive pathways act to control infection. In many cases, this response outbreaks the goal and induces multiple organ failure. Energetic and protein stores are overlaped. Then **nutritional** support is one of the way by which outcome may improve. Some **nutrients** have pharmacological properties which can modulate response to stress. This new therapeutic prospect includes new lipid substrates (fish oil, structured lipids, medium-chain triglycerides), amino acids (**glutamine**, **arginine**) and free radical scavengers (vitamines, trace elements or enzyme-dependant). Enteral **nutrition** is probably the best way for **nutritional** support in this disease.

L24 ANSWER 37 OF 45 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 94:222445 SCISEARCH
THE GENUINE ARTICLE: NF168
TITLE: STRATEGIES FOR ATTENUATING PROTEIN-CATABOLIC RESPONSES IN THE CRITICALLY ILL
AUTHOR: ZIEGLER T R (Reprint); GATZEN C; WILMORE D W
CORPORATE SOURCE: BRIGHAM & WOMENS HOSP, DEPT MED, 1 JOSLIN PL, BOSTON, MA, 02215 (Reprint); ST MARYS HOSP, DEPT SURG, LONDON W2 1NY, ENGLAND; BRIGHAM & WOMENS HOSP, DEPT SURG, BOSTON, MA, 02115; BRIGHAM & WOMENS HOSP, SURG METAB & NUTR LAB, BOSTON, MA, 02115; HARVARD UNIV, SCH MED, BOSTON, MA, 02115; HARVARD UNIV, JOSLIN DIABET CTR, SCH MED, BOSTON, MA, 02215
COUNTRY OF AUTHOR: USA; ENGLAND
SOURCE: ANNUAL REVIEW OF MEDICINE, (1994) Vol. 45, pp. 459-480.
ISSN: 0066-4219.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH

Search completed by David Schreiber 308-4292

REFERENCE COUNT: 73

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Specialized enteral and parenteral **nutrition** are now a standard components of care in critically ill patients. This adjunctive therapy corrects and prevents **nutrient** deficiencies, attenuates the loss of body protein, and improves clinical outcomes in malnourished patients. Several novel strategies designed to improve the metabolic and clinical effects of specialized **nutrition** are under vigorous clinical investigation.

These new approaches include increased emphasis on enteral feeding to maintain intestinal absorptive, immune, and barrier function; adminstration of conditionally essential amino acids (**glutamine**, **arginine**); use of specialized lipid products and antioxidants; and administration of growth factors such as human growth hormone. Randomized, controlled clinical trials will define the clinical and metabolic efficacy and cost-effectiveness of these therapies in specialized **nutrition** support.

L24 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:34184 HCAPLUS
DOCUMENT NUMBER: 118:34184
TITLE: Conformational and aggregational states of .omega.-aminoacylmelittin derivatives
AUTHOR(S): Ramalingam, Kalaiyarasi; Bello, Jake
CORPORATE SOURCE: Dep. Chem., State Univ. New York, Buffalo, NY, 14263, USA
SOURCE: Biochemistry (1993), 32(1), 253-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors detd. the effect of displacing the pos. charges of the amino groups of N-terminal glycine and lysine residues away from the backbone of melittin in coil-to-helix transitions by using .omega.-aminoacyl derivs. of melittin. These were prepd. by acylating the amino groups of melittin with .omega.-amino acids to yield the melittin derivs. glycylmelittin (MLT-2), (4-aminobutanoyl)melittin (MLT-4), and (5-aminopentanoyl)melittin (MLT-5), resp. At pH 7.2, there is a chain-length-dependent increase in helicity from MLT to MLT-5. The .omega.-aminoacylmelittin derivs. also show a concn.-dependent increase in helicity at pH 7.2. However, at pH 2.3, a concn.-independent, but chain length-dependent increase in helicity was obsd. A hydrophilic deriv. glycylglycylmelittin (MLT-GG) and a hydrophobic deriv. MLT-5, which have side chains of equal length, show similar helicity, at pH 7.2, but at pH 2.3 MLT-GG shows almost no helicity, while MLT-5 is about 60% helical. The lysyl deriv. (MLT-K), which has addnl. pos. charges compared to melittin, behaves much like MLT-2. At pH 7.2, all the derivs. exhibit both cold- and heat-induced denaturation; a significant amt. of residual structure is retained in the temp. range 80-100.degree.. These results are discussed in terms of the electrostatic and hydrophobic interactions involving the side chains.

L24 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:192247 HCAPLUS
DOCUMENT NUMBER: 118:192247
TITLE: Purification of synthetic peptides using reversible chromatographic probes based on the Fmoc molecule
AUTHOR(S): Ball, H. L.; Mascagni, P.
CORPORATE SOURCE: Italfarmaco Res. Cent., Milan, Italy
SOURCE: International Journal of Peptide & Protein Research (1992), 40(5), 370-9

Search completed by David Schreiber 308-4292

CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid, reversible procedure for purifying synthetic peptides has been developed based on the specific incorporation of 9-(4-carboxyfluorenyl)methoxycarbonyl (4-COR-Fmoc; R = lipophilic or charged group) group onto the terminal amino acid of peptidyl resins. The acid-stable 4-COR-Fmoc derivs. were synthesized with a variety of chem. groups, thus altering the chromatog. properties of the target peptides and permitting their convenient purifn., either by reversed-phase HPLC or ion exchange chromatog. The assembly of the peptides involved a capping step to prevent the formation of deletion forms. The 4-COR-Fmoc derivs. were incorporated either as preformed amino acid conjugates or as activated succinimidyl esters. After HF cleavage and purifn., the 4-COR-Fmoc probes were quant. removed with org. bases. The efficiency of the technique was demonstrated by the purifn. of small- to large-sized peptides, including a cyclic analog.

L24 ANSWER 40 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:332692 BIOSIS
DOCUMENT NUMBER: BA94:34533
TITLE: THE METABOLIC EFFECTS OF THERMAL INJURY.
AUTHOR(S): TREDGET E E; YU Y M
CORPORATE SOURCE: 2D3.82 WALTER MACKENZIE CENTRE, UNIV. ALBERTA HOSP., EDMONTON, ALBERTA T6G 2B7, CAN.
SOURCE: WORLD J SURG, (1992) 16 (1), 68-79.
CODEN: WJSUDI. ISSN: 0364-2313.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Major thermal injury is associated with extreme hypermetabolism and catabolism as the principal metabolic manifestations encountered following successful resuscitation from the shock phase of the burn injury. Substrate and hormonal measurements, indirect calorimetry, and nitrogen balance are biochemical metabolic parameters which are useful and more readily available biochemical parameters worthy of serial assessment for the metabolic management of burn patients. However, the application of stable isotopes with gas chromatography/mass spectroscopy and more recently, new **immunoassays** for growth factors and cytokines has increased our understanding of the metabolic manifestations of severe trauma. The metabolic response to injury in burn patients is biphasic wherein the initial ebb phase is followed by a hypermetabolic and catabolic flow phase of injury. The increased oxygen consumption/metabolic rate is in part fuelled by evaporative heat loss from wounds of trauma victims, but likely also by a direct central effect of inflammation upon the hypothalamus. Although carbohydrates in the form of glucose appear to be an important fuel source following injury, a maximum of 5-6 mg/kg/min only is beneficial. Burn patients have accelerated gluconeogenesis, glucose oxidation, and plasma clearance of glucose. Additionally, considerable futile cycling of carbohydrate intermediates occurs which includes anaerobic lactate metabolism and Cori cycle activity arising from wound metabolism of glucose and other substrates. Similarly, accelerated lipolysis and futile fatty acid cycling occurs following burn injury. However, recent evidence suggests that lipids in the diet of burned and other injured patients serve not only as an energy source, but also as an important **immunomodulator** of prostaglandin metabolism and other **immune** responses. Amino acid metabolism in burn patients is characterized by increased oxidation, urea synthesis, and protein breakdown which is prolonged and difficult to reduce with current **nutritional** therapy. However, the current goal of

**nutritional** support is to optimize protein synthesis. Specific unique requirements may exist for supplemental glutamine and arginine following burn injury but further research is needed before enhanced branched chain amino acids supplements can be recommended for burn patients. Recent research investigations have revealed the importance of enteral feeding to enhance mucosal defense against gut bacteria and endotoxin. Similarly, research has demonstrated that many of the metabolic perturbations of burns and sepsis may be due, at least in part, to inflammatory cytokines. Investigation of their **pathogenesis** and mechanism of action both at a tissue and a cellular level offer important prospects for improved understanding and therapeutic control of the metabolic disorders of burn patients.

L24 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:578293 HCAPLUS
DOCUMENT NUMBER: 113:178293
TITLE: Parenteral nutrients containing L-glutamine oligopeptides
INVENTOR(S): Kosegi, Koji; Tsukamoto, Zenji; Kuniba, Yukifumi; Yaginuma, Hideya; Sato, Makoto
PATENT ASSIGNEE(S): Morishita Pharmaceutical Co., Ltd., Japan; Ajinomoto Co., Inc.
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 02119762 | A2 | 19900507 | JP 1988-270557 | 19881025 |

PRIORITY APPLN. INFO.: JP 1988-165500 19880701

AB Parenteral nutrients contain essential and nonessential amino acids and at least one peptide selected from di- and/or tripeptides contg. L-isoleucine 4.0-13.0, L-leucine 10.0-20.0, L-lysine 3.5-13.0, L-methionine 1.5-10.0, L-phenylalanine 3.0-10.0, L-threonine 3.0-11.0, L-tryptophan 0.5-5.0, L-valine 3.0-14.5, L-arginine 3.0-12.0, L-histidine 2.0-7.0, glycine 2.0-12.0, L-alanine 3.0-15.0, L-cysteine 0-1.0, L-aspartic acid 0-4.0, L-glutamic acid 0-7.0, I 5.0-40.0, L-proline 1.5-5.5, L-serine 0.5-3.0, and L-tyrosine 0.1-5.0 g/100 g total amino acids (the oligopeptides are reduced as amino acids) and with wt. ratio of [total branched amino acids (A)]/glutamine = 0.11-7.50, A/(total amino acids) = 0.18-0.46, and (total nonessential amino acids)/(total essential amino acids) = 0.50-1.80. Ala-Gln 24.2, isoleucine 7.6, leucine 10.8, lysine 5.9, methionine 3.7, phenylalanine 5.8, threonine 6.3, tryptophan 1.1, valine 9.3, arginine 6.5, aspartic acid 0.8, glutamic acid 0.4, histidine 4.2, proline 4.2, serine 1.4, tyrosine 0.3, and glycine 5.5 g were mixed with H2O to 1 L (pH 6.5), filtered, charged into vials, and sterilized to give an i.v. infusion soln., which showed better nutritious effect in rats than glutamine-free control.

L24 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:476321 HCAPLUS
DOCUMENT NUMBER: 95:76321
TITLE: Laser ionization mass spectrometry of nonvolatile samples
AUTHOR(S): Hardin, E. D.; Vestal, M. L.
CORPORATE SOURCE: Dep. Chem., Univ. Houston, Houston, TX, 77004, USA

SOURCE: Anal. Chem. (1981), 53(9), 1492-7
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new laser ionization mass spectrometer was developed which uses a moving stainless-steel belt onto which the sample is electrosprayed for continuous sample introduction. Ionization is produced by focusing the output of a tunable dye laser onto the moving belt. The mass spectrometer system is a conventional quadrupole system, with the exception of a gated boxcar integrator to process the pulsed ion beam. Mass spectra were recorded for a no. of nonvolatile biomols. including saccharides, amino acids, peptides, nucleosides, and nucleotides. Generally these spectra show intense cationized mol. ions, often including multiple alkali addn., and little fragmentation. The major limitation of the technique at present is the poor reproducibility of the spectra. Ion time-of-flight distributions were measured which show that ions produced by laser desorption/ionization have broad kinetic energy distributions with most probable kinetic energies of .apprx.6 eV and with high-energy tails extending beyond 25 eV. The time-of-flight distributions also show that most of the high-mass ions obsd. result from metastable decompn. of larger clusters formed initially at the surface.

L24 ANSWER 43 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 15

ACCESSION NUMBER: 1981:155243 BIOSIS
DOCUMENT NUMBER: BA71:25235
TITLE: **MUSCLE** AND PLASMA AMINO-ACIDS FOLLOWING INJURY INFLUENCE OF INTERCURRENT INFECTION.
AUTHOR(S): ASKANAZI J; CARPENTIER Y A; MICHELSEN C B; ELWYN D H; FURST P; KANTROWITZ L R; GUMP F E; KINNEY J M
CORPORATE SOURCE: DEP. ANESTHESIOL., COLL. PHYSICIANS SURG., COLUMBIA UNIV., NEW YORK, N.Y. 10032, USA.
SOURCE: ANN SURG, (1980) 192 (1), 78-85.
CODEN: ANSUA5. ISSN: 0003-4932.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Intracellular amino acid patterns in patients with multiple trauma, whether or not complicated by sepsis and during convalescence were studied. A percutaneous **muscle** biopsy was performed 3-4 days following major accidental injury in 10 patients and analyzed for **muscle** free amino acids. Venous blood was drawn at the time of the biopsy and analyzed for plasma free amino acids. Five patients developed sepsis and a repeat biopsy was performed on days 8 to 11. In 5 of the patients a biopsy was performed during the late convalescent period (anabolic phase). A marked depletion of nonessential amino acids in **muscle** occurred in injury and sepsis due to a decrease (50%) in glutamine, which was equally marked in both states. The essential amino acids in **muscle** increased in injury. During sepsis, a further increase was observed with a return toward normal in the convalescent period. In injury, the most marked rise was in the branched-chain amino acids, phenylalanine, tryosine and methionine. With sepsis, a further rise in **muscle** branched-chain amino acids, phenylalanine and tryosine occurred, while plasma levels remain unchanged. During convalescence, **muscle glutamine**, **arginine**, histidine and plasma branched-chain amino acids were below normal, whereas **muscle** phenylalanine and methionine were elevated. The **muscle** free amino acid pattern observed after major trauma was essentially the same as earlier described following elective operation. A common response of intracellular amino acids irrespective of the degree of

injury was suggested, and the pump settings which regulate amino acid transport follow the 'all or none' rule. The high intracellular levels of branched-chain amino acids in sepsis suggest that the energy deficit of this state is due to an impairment of substrate use rather than intracellular availability. The high concentrations of the aromatic amino acids and methionine may be due to altered liver function. During the late convalescent period (anabolic phase) the low levels of certain key amino acids suggests inadequate **nutrition**. The difficulties in nourishing the injured or septic patient are well recognized. The period following these catabolic states may be an important period for the application of an optimal, aggressive **nutritional** regimen. [ **Muscle** wasting was discussed.]

L24 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:167528 HCAPLUS
DOCUMENT NUMBER: 86:167528
TITLE: Amino acids and peptides in seven species of green marine algae
AUTHOR(S): Miyazawa, Keisuke; Ito, Keiji; Matsumoto, Fumio
CORPORATE SOURCE: Fac. Fish. Anim. Husb., Hiroshima Univ., Fukuyama, Japan
SOURCE: Hiroshima Daigaku Suichikusan Gakubu Kiyo (1976), 15(2), 161-9
CODEN: HIDGAW
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid compns. of 7 marine green algal exts. were examd. by an amino acid analyzer. Ulva pertusa contd. a large amt. of L-arginyl-L-glutamine. This peptide was also detected in Enteromorpha linza, but not in the other 5 species. Relatively high levels of glutamate and glutamine were found in Codium fragile, Codium adhaerens, and Chlorodesmis comosa. The level of glycine in Caulerpa racemosa was markedly high. Glycine and proline were predominant in Cladophora densa. Aminosulfonic acids in these algae were examd. by paper chromatog. Taurine was detected in 4 species, D-cysteinolic acid in 3, N-monomethyltaurine in 2, and homotaurine in 1. Occurrence of homotaurine in Cladophora densa was also confirmed.

L24 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:501610 HCAPLUS
DOCUMENT NUMBER: 81:101610
TITLE: Molecular biology of Euglena gracilis. IX. Amino acid pool composition
AUTHOR(S): Kempner, E. S.; Miller, J. H.
CORPORATE SOURCE: Natl. Inst. Arthritis, Metab., Dig. Dis., Natl. Inst. Health, Bethesda, Md., USA
SOURCE: J. Protozool. (1974), 21(2), 363-7
CODEN: JPROAR
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid compn. of the acid-sol. fraction of E. gracilis was detd. from cells grown in 4 different culture media. Glutamic acid was the major free amino acid. Hydrolysis of this fraction increased the amt. of free amino groups; major acids found were glutamic acid, aspartic acid, glycine, and arginine. The distribution pattern was similar in the 4 cultures. L-Arginyl-L-glutamine was isolated and identified in the 4 cultures and was a metabolic intermediate.